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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,726	07/16/2004	Renate Kunert	3224-153	4370

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EXAMINER	
PARKIN, JEFFREY S	

ART UNIT	PAPER NUMBER
1648	

NOTIFICATION DATE	DELIVERY MODE
04/30/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/501,726	KUNERT ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-10,13 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-3,6-10 and 19* is/are allowed.

6)☒ Claim(s) *13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Office Action

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the communication filed 06 February, 2009. Claims 1-3, 6-10, 13, and 19 are pending in the instant application.

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The previous rejection of claims 1-3, 6-10, 13, and 19 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is hereby withdrawn in response to applicants' amendment and arguments.

Allowable Subject Matter

Claims 1-3, 6-10, and 19 appear to be free of the prior art of record.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claim 13 stands rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 13 is directed toward a **pharmaceutical composition** or **vaccine** comprising an anti-idotypic antibody to 2F5. The term "pharmaceutical" has an art-recognized meaning and references any chemical compound used on or administered to humans or animals as an aid in the diagnosis, treatment, or prevention of disease or other abnormal condition, for the relief of pain or suffering, or to control or improve any physiologic or pathologic condition [see Dorland's Medical Dictionary at http://www.mercksource.com/pp/us/cns/cns_hl_dorlands.jspzQzpgzEzzSzppdocszSzuszSzcommonzSzdorlandszSzdorlandzSzdmd_d_29zPzhtm#12313424 or the San Francisco AIDS Foundation Glossary of HIV/AIDS Terms at http://www.sfaf.org/custom/glossary.aspx?l=en&a=P]. the term "vaccine" has an art-recognized meaning and referencres a composition administered to stimulate an immune response; vaccines typically include killed or attenuated (weakened or inactivated) microorganisms, their proteins, or genetically engineered pieces (subunits). A preventive (prophylactic)

vaccine is used to prevent initial infection, while a therapeutic (treatment) vaccine is given after infection to enhance the body?s immune response and arrest disease progression or reduce its severity. [see Dorland's Medical Dictionary at http://www.mercksource.com/pp/us/cns/cns_hl_dorlands_split.jsp?pg=/ppdocs/us/common/dorlands/dorland/eight/000113869.htm or the San Franciso AIDS Foundation Glossary of HIV/AIDS Terms at http://www.sfaf.org/custom/glossary.aspx?l=en&a=V]. Thus, the claimed composition must be useful as either a vaccine or drug for the prevention and treatment of HIV infection.

The premise of the invention is directed toward the administration of an anti-idiotypic antibody (Ab2) to a patient. Ab2 was generated against an HIV-1 neutralizing Mab (Ab1) designated Mab 2F5. Thus, Ab2 upon administration to patients may act as a competitive/noncompetitive inhibitor of Ab1 or it may act as an antigen to induce the formation of anti-anti-idiotypic antibodies (Ab3) that have similar properties to the parental antibody (Ab1). Moreover, the disclosure states that "In principle, Ab2 beta antibodies raised against antibodies neutralizing HIV-1 might have an enormous potential for vaccine design" (p. 3). Thus, applicants are clearly interested in employing the claimed compositions as immunogens in a vaccinating composition.

As previously set forth, the legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth. *Enzo Biochem, Inc.*, 52 U.S.P.Q.2d 1129 (C.A.F.C. 1999). *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988). *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries

should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

1) The disclosure fails to provide adequate guidance pertaining to the correlates of human protection and methods for eliciting protective/therapeutic immune responses. To date, it is not currently known what type of immune response will provide a protective/therapeutic outcome.

2) The disclosure fails to provide any guidance pertaining to the immunologic/pharmacologic properties of any given therapeutic Mab. The disclosure fails to provide detailed guidance pertaining to the binding specificity, coding potential, affinity, specificity, titer, and pharmacological profile of any given therapuetic Mab.

3) The disclosure fails to provide any working embodiments demonstrating that administration of an anti-idiotypic antibody (e.g., Mab 3H6) or an anti-anti-idiotypic antibody is capable of providing a therapeutic or protective outcome. Considering the unpredictability of the prior art, multiple working embodiments would be required to enable the claimed invention. However, the specification fails to provide any data pertaining to the administration of Ab2 or the generation of therapeutic Ab3.

4) The state-of-the-art vis-à-vis HIV vaccine development is one of unpredictability (Moore and Burton, 1999; Haynes *et al*.,

2005; Montefiori, 2005; Trkola *et al*., 2005; Gallo, 2005; Walker and Burton, 2008). Several problems have hampered the development of an efficacious HIV vaccine including the following: 1) The correlates of human protection remain to be elucidated. 2) It is not readily manifest which immunogens, carriers, adjuvants, and immunization regimen should be employed in the generation of a therapeutic/prophylactic immune response. 3) There are currently no animal models that allow direct extrapolations of vaccine efficacy. 4) HIV-1 and -2 exist as a quasispecies that leads to immune avoidance and rapid immune escape. 5) HIV can reside in a number of different reservoirs in a latent state, thereby avoiding detection. 6) It is not readily manifest how to generate a long-lasting high-titer immune response to HIV.

Moore and Burton (1999) suggests that it might not be possible to generate Nabs of the requisite titer and specificity to effectively combat HIV-1 infection. This is because experimental animal data suggests that partial neutralization (i.e., 90% neutralization) is insufficient to inhibit HIV-1 infection. It may well require 100% neutralization, a figure not currently seen. Haynes *et al*. (2005) identifies some of the problems with using Nab 2F5 as a target. This Mab is a polyspecific autoantibody that also reacts with the phospholipid cardiolipin. The author concluded (see Abstract, p. 1906) that "current HIV-1 vaccines may not induce these types of antibodies because of autoantigen mimicry of the conserved membrane-proximal epitopes of the virus." Trkola et al. (2005) note that it will be difficult to generate high-titer Nabs with the desired specificity. Moreover, the vast majority of patients in a passive antibody study displayed viral rebound and immune

escape in a short period of time. Thus, it is not readily manifest how effective Nabs will be at combating HIV-1 infection. Montefiori (2005) also concluded that it will be extremely difficult to generate high-titer Nabs with the desired specificity.

Accordingly, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention.

Response to Arguments

Applicants traverse the rejection and submit that the preparation of pharmaceutical compositions and vaccines comprising the antibody of claim 13 is "within the general knowledge of the ordinarily skilled artisan in the field of immunology/vaccine development" (see p. 10). It was further argued that only routine experimentation would be required to practice the claimed invention. These arguments are not deemed to be persuasive for the reasons of record set forth *supra* in the preceding rejection. The crux of the rejection is not whether or not the claimed composition can be prepared, but whether the claimed composition would reasonably be expected to function as a vaccine or pharmaceutical. As discussed above, several factors have precluded the development of a successful HIV vaccine or hindered the development of efficacious antivirals. Applicants' response failed to proffer any data or publications addressing those concerns. Accordingly the rejection is proper and hereby maintained.

Action Is Final

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Larry R. Helms, can be reached at (571) 272-0832. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent

related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

/Jeffrey S. Parkin/

Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

26 April, 2009